in the overall control patients, 113.20 ± 89.8% in the matched control patients ($p < 0.01$; patients with high Lp(a) levels vs overall and matched controls). Maximal increases in the coronary diameter had negative correlations with Lp(a) levels ($p < 0.05$, $r = -0.25$ and -0.35; patients with high Lp(a) levels vs overall and matched controls, respectively). Maximal increases in the coronary blood flow had also negative correlations with Lp(a) levels ($p < 0.01$, $r = -0.31$ and -0.49, patients with high Lp(a) levels vs overall and matched controls, respectively). These results suggested elevated Lp(a) levels impair endothelium-dependent vasodilator response, which may contribute to accelerated atherogenic or thrombogenic processes in patients with high Lp(a) levels.

1045-19 Comparative Effect of Pravastatin and Simvastatin on Platelet-Thrombus Formation in Hypercholesterolemic Coronary Patients

Lucie Lacoste, Jules Y.T. Lam. *Montreal Heart Institute, Montreal, Quebec, Canada*

High cholesterol (chol) is a risk factor for coronary atherosclerosis and reducing elevated cholesterol has been shown to prevent coronary morbidity and mortality. Hypercholesterolemic pts also have hyperactive platelets and an increased tendency to platelet-thrombus formation at the site of an injured arterial wall. This prothombotic tendency may favor the development of acute ischemic coronary events due to coronary thrombosis at the site of plaque rupture. Whether, reduction of serum cholesterol with the HMG-CoA reductase inhibitors, pravastatin (Prava) or simvastatin (Simva), will influence platelet thrombosis in stable coronary pts taking aspirin, 325 mg/day, was assessed before and after 2–3 months of Prava therapy (40 mg/day, n = 16) or Simva therapy (20 mg/day, n = 16). Platelet thrombus formation (PT) was evaluated by exposing porcine aortic media (simulating deep arterial injury) to the pt's flowing venous blood for 3 min at shear rates of 2546 and 754 s^{-1} at 37°C in a superfusion chamber ex vivo. Serum lipids and quantitative morphometric PT (μm^2/mm) before and after drug treatment are shown below:

	Shear rate	Basal	Prava	Basal	Simva
PT:	2546 s^{-1}	2.0 ± 0.4	1.0 ± 0.2*†	2.1 ± 0.4	2.0 ± 0.4
	754 s^{-1}	1.7 ± 0.4	0.9 ± 0.1*†	1.8 ± 0.4	1.8 ± 0.4
Chol:	Total	6.1 ± 0.1	4.6 ± 0.2*	6.5 ± 0.3	4.7 ± 0.2*
(mmol/L)	LDL	4.1 ± 0.1	2.8 ± 0.1*	4.5 ± 0.3	2.8 ± 0.2*

*$p < 0.05$ vs basal, †$p < 0.05$ vs Simva

Thus, both Simva and Prava decreased serum total and LDL cholesterol, but platelet thrombosis was inhibited more by Prava at both the high and low shear rates tested. These results suggest that after 2–3 months of therapy, HMG-CoA reductase inhibitors may have a differential effect on platelet thrombosis which may influence the early clinico-pathologic evolution of the coronary atherosclerotic process.

1045-20 Immune Responses to HMG-CoA Reductase Inhibitors in Patients With Abnormal Lipid Level

Minh N. Bui, Michael T. Caulfield, Paul Katz, Richard O. Cannon III, Charles E. Rackley. *Georgetown University Medical Center, Washington, DC; NHLBI, NIH, Bethesda, MD*

Clinical trials with HMG-CoA reductase inhibitors have reported decrease in clinical events out of proportion to small anatomical changes in coronary angiogram. Previous finding from our lab has shown that HMG-CoA reductase inhibitors cause a rise in IgG autoantibodies to oxidized LDL(ox-LDl) during the first 6 months of therapy. However, the autoantibodies titers decrease by 12 months. We examined the potential immune response in hyperlipidemic patients treated with HMG-CoA reductase inhibitors. A nonisotopic ELISA technique was used to measure autoantibodies titers in 11 patients with hyperlipidemia. LDL, IgG and IgM autoantibodies titers were measured at baseline and at 4 ± 1.4 months after treatment with HMG-CoA reductase inhibitors.

	Baseline	4 months
LDL (mg/dl)	173 ± 37	138 ± 28*
Autoantibodies to ox-LDL (OD)		
IgG	0.138 ± 0.076	0.154 ± 0.087
IgM	0.024 ± 0.019	0.053 ± 0.044*

*p-value < 0.05 vs. baseline by paired Student t-test; OD: optical density

Conclusion: 1) A decrease in LDL level was associated with an increase in autoantibodies titers to ox-LDL. 2) Early increase in autoantibodies titers was greater with IgM than IgG. 3) These early immune responses may contribute to plaque stabilization.

1045-21 Percent Cholesterol Absorption in Normal Human Subjects by Negative Ion Gas Chromatography Mass Spectrometry

Matthew S. Bosner, William Stenson, Patricia Turnbough, Stephen Block, Laura Kobayashi, Abigail Schweizer, Richard E. Ostlund, Jr.. *Jewish Hospital and Washington University School of Medicine, St. Louis, MO*

Percent cholesterol (CH) absorption was measured in 70 normal subjects on their ambient diet by simultaneous administration of 30 mg CH [23,24,25,26,27]^{13}-C5–CH orally with a standard meal and 15 mg [26,26,26,27,27,27]^{2}-H6–CH IV. Blood was collected on days 0 and 3, CH isolated, and derivatized to a pentafluorobenzoyl ester, and the ratio of isotopic tracer analyzed by negative ion gas chromatography mass spectrometry. The resulting mass spectra consisted almost solely of intense molecular CH ions permitting detection of 20 fmol of tracer. Percent CH absorption was 56.8 ± 11.5% (mean ± SD, N = 70, age 18 to 82 years, 51 female, 19 male), confirming heterogeneity of CH absorption in normal humans. CH absorption was not related to age, gender, plasma, lipids or apoprotein levels including apo-E genotype (by PCR). Chronic dietary calories, dietary % fat or CH composition, or fiber quantitated from 7-day food records were not related to CH. CH was significantly negatively correlated with plasma insulin ($r = -0.280$, $p = 0.049$) and plasma C-peptide (-0.25, $p = 0.0079$). Thus percent CH absorption may be regulated by insulin and altered by insulin resistance. The SD between tests performed 4–6 weeks apart was 2.8% suggesting stability over time. This novel and broadly applicable method may provide a precise technique to quantify interventions such as diet or drugs on CH absorption in humans.